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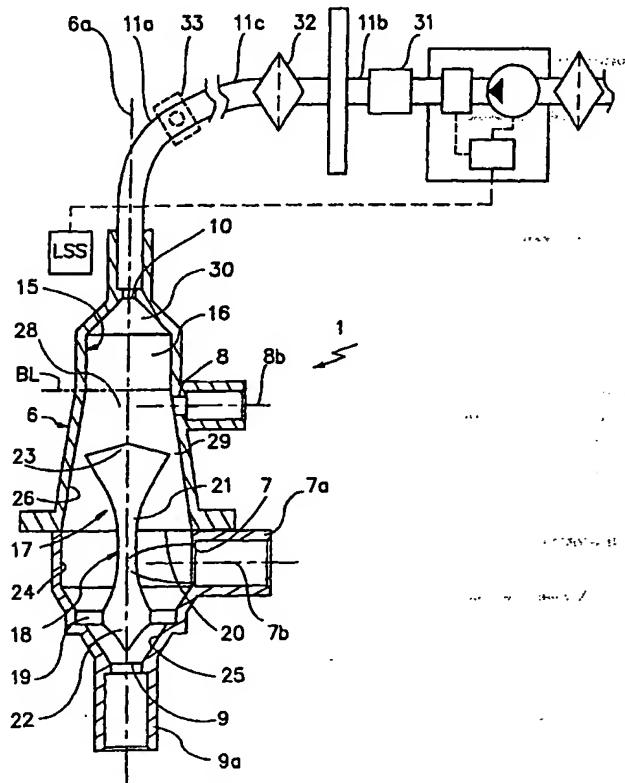
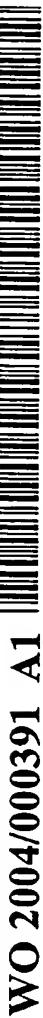
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(54) Title: GAS SEPARATION DEVICES



(57) Abstract: A description is given of a gas separation device for a physiological fluid, comprising a containing body (6) having at least a first inlet aperture (7) for a physiological fluid, positioned with a tangential direction of access, at least one outlet aperture (9) for the said fluid, spaced apart from the said inlet aperture, and a guide element (17) housed within the said body. The guide element (17) has a continuous active surface (15) designed to contact and guide the said fluid and delimits, together with the containing body (6), a first annular chamber (20) into which the first inlet aperture (7) opens directly.

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GAS SEPARATION DEVICES

DESCRIPTION

Background of the Invention.

The present invention relates to a gas separation device
5 for physiological fluids, particularly for cellular fluids such as blood. The present invention relates also to a fluid mixing device with gas separation.

It is known that any gas particles present in a physiological fluid, such as blood circulating in an
10 extracorporeal circuit, must be effectively removed when the fluid is to be administered to a patient. It should be pointed out that this is because excessively large gas particles can be dangerous if they are transferred to a patient's cardiovascular system.

15 It is also known that some treatments require the simultaneous administration to a patient of both a physiological fluid, for example blood circulating in an extracorporeal circuit, and an additional fluid, for example an infusion or replacement liquid. However, before
20 the two fluids, for example blood and infusion liquid, are transferred to the patient, it is necessary to remove any gas particles that may be present.

This document makes reference, without restrictive intent, to the field of machines for extracorporeal blood
25 treatment, such as dialysis machines, in which field there is a known method of using at least one gas separation device operating in a line for the return of blood to the patient.

A gas separation device suitable for the application
30 described above comprises, typically, a containing body providing within itself a chamber designed to be partially occupied by the blood which is to undergo the degassing operation. Suitable shaping of the chamber allows the blood

to accumulate in a lower part of the chamber, thus promoting the separation of the gas bubbles. These bubbles can be removed through a service line or discharged directly to the exterior.

- 5 Normally, the pressure within the separation device is kept below atmospheric pressure, in order to promote the separation of the air bubbles.

The blood leaving the device described above then passes through an air bubble sensor which, in turn, can operate a
10 safety clamp. The clamp is typically positioned on the line returning the blood to the patient, in order to prevent any event considered to be dangerous from being propagated into the patient's cardiovascular system.

Another gas separation device of a known type is
15 illustrated in US Patent No. 5707431. This device comprises a cylindrical chamber divided radially into two parts by a filter, also cylindrical, located centrally in the chamber.

The blood inlet is located in a top part of the chamber and is directed tangentially towards the outer part of the
20 chamber to create a vortex flow. The vortex flow of blood in the outer part of the chamber is converted to an essentially vertical flow as a result of the passage of the fluid through the cylindrical filter. The blood proceeds downwards and passes out through an aperture in the lower
25 part of the separation chamber.

The air bubbles, which because of the vortex motion of the blood tend to move towards a perimetric area of the chamber, move upwards towards a hydrophobic membrane which is located at the top of the chamber and which allows the
30 gas to be discharged to the external atmosphere.

Finally, a one-way valve located next to the membrane prevents the air from returning into the chamber.

The following publications:

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- FR 2,508,319;
 - EP 0 661 063;
 - US 5,421,815;
 - JP 90-182404;
- 5 - "Interaction of blood and air in venous line air trap chamber", extract from Artificial Organs (vol. 14, suppl. 4), K. Ota and T. Agishi, ICAOT Press, Cleveland 1991, pp. 230-232; and
- 10 - ASAIO Journal (1993), "Suppression of thrombin formation during hemodialysis with triglyceride"

disclose the use of a layer of fluid interposed between the free surface of the blood and the air, in order to reduce the appearance of coagulation phenomena.

15 In particular, EP 0 661 063 and US 5,421,815 illustrate a blood/air separation chamber comprising a tubular containing body provided with a top cover to which a blood inlet tube is connected. In the described chamber, the blood accumulates in a lower part of the tubular body; in order to separate the blood from direct contact with the 20 air, a static layer of anticoagulant material is used, comprising triglyceride acids and an antioxidant interposed between the free surface of the blood and the air. Since this static layer is carried on the surface and is only miscible with difficulty with the blood, it prevents direct 25 contact between the blood and the air.

Finally, document WO 00/32104 discloses a pressure sensing system in which a service tube, partially filled with a cell-free solution, is interposed between a pressure sensor and a blood circuit. The cell-free solution creates a 30 separating column between the blood and air which, because of the small section of the service tube, prevents or reduces to a minimum the propagation of one or more

components of the blood towards the end of the service tube which is occupied by the air.

The technical solutions described above have been found to have certain aspects that could be improved.

- 5 In the first place, many of the devices mentioned have large blood-air interfaces which, as is known, promote the formation of clots and encrustations, or, alternatively, in solutions using a static layer to separate the air from the blood, require the use of chemical substances immiscible
10 with blood which float on the surface of the blood to prevent its direct contact with the air.

In the second place, the devices mentioned are not capable of both efficiently mixing the blood with any infusion or replacement fluid that may be present and simultaneously
15 and effectively degassing both fluids.

It should also be noted that the conventional solutions require the presence of a relatively high volume within the gas separation device; in the case of dialysis treatment, for example, the quantity of blood constantly occupying the
20 interior of the separation device increases to a considerable and undesired extent the total amount of blood kept outside the patient.

It should also be noted that, if a tangential blood inlet is to be used to create a vortex to promote the separation
25 of air bubbles from the blood according to the known method, it is necessary to have a central filter to prevent the transfer of the air bubbles to the exit of the separator. The presence of the filter not only increases the overall cost of the device, but also constitutes an
30 additional element which may lead to encrustation and undesired deposits of particles, particularly when part of the filter is located in an air-blood interface area.

Moreover, the known devices which have been described are relatively unsuitable for permitting high blood flows (of

the order of 500 ml/min.), low pressure drops and absence of stagnation points, with simultaneous and effective mixing of any infusion liquid.

Summary of the Invention.

- 5 The object of the present invention is to provide a gas separation device for a physiological fluid, for example blood, which is capable of operating effectively even at high flow rates, while minimizing the total volume of blood that is to be held within the said device.
- 10 A further object of the invention is to provide an optimal quality of the flow through the gas separation device, by essentially eliminating the presence of stagnation points and reducing pressure drops to a minimum.
- 15 Another object of the invention is a gas separation device made in such a way that the flow leaving the said device is not capable of generating undesired phenomena of return of gas bubbles towards the outlet of the device.
- 20 Another object of the invention is to provide a gas separation device capable of offering an optimal area for access by at least one infusion line, thus permitting an efficient mixing of the blood with the infusion fluid while carrying out effective and simultaneous separation of any gas from the infusion fluid and from the blood, and while minimizing the air-blood interface.
- 25 A further object of the present invention is to provide a fluid mixing device with gas separation, capable of operating effectively even at high flow rates, while minimizing the air-blood interface.
- 30 The invention also has the object of reducing to the smallest possible level the total volume of blood occupying the said device.

Another object of the invention is to provide a device for actively adjusting the thickness of a layer of infusion liquid lying above the blood or other cellular fluid.

5 The objects outlined above are essentially achieved by a device according to one or more of the attached claims.

Brief Description of the Drawings.

10 Further characteristics and advantages will be demonstrated by the detailed description of a preferred, but not exclusive, embodiment of a device according to the present invention.

This description is given below, with reference to the attached drawings, provided purely for guidance and therefore without restrictive intent, in which:

- 15 Figure 1 is a view in longitudinal section, showing the device according to the invention in a vertical position similar to that in which it is used;
- Figure 2 shows a longitudinal section through an upper half of the containing body of the device according to the invention;
- 20 Figure 3 shows a longitudinal section through a lower half of the containing body of the device according to the invention;
- Figure 4 is a view through the line IV-IV in Figure 2;
- Figure 5 is a view through the line V-V in Figure 3;
- 25 Figure 6 shows a blood treatment line using the device according to the invention;
- Figure 7 shows a plan view of a detail of Figure 1.

Detailed Description.

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With reference to Figure 1, the number 1 indicates a fluid mixing device with gas separation.

As shown in Figure 6, the device 1 can operate in a disposable line 2 for extracorporeal blood treatment,
5 comprising a branch 3 for withdrawing the blood from the patient, a blood treatment unit 4 and a branch 5 for returning the blood to the patient.

In greater detail, the unit 4, a dialysis filter for example, is interposed between the two branches 3 and 5,
10 while the device 1 operates on the return branch 5, up-line from the point of access to the patient's vascular system.

The device 1 comprises a containing body 6, having a longitudinal axis of symmetry 6a; the body 6 forms an internal volume 16 which is designed to receive a specified
15 quantity of fluid and which has a radial dimension significantly larger than that of the branches 3 and 5, so that the velocity of the said fluid is decreased and the gas is efficiently separated, as described below.

In operating conditions, both the device 1 and the
20 treatment 4 are positioned with their longitudinal axes orientated vertically, although the device can in fact operate with its longitudinal axis inclined.

The fluid, for example blood, flowing through the line 3 passes through the unit 4 with a vertical upward motion and
25 then enters the device 1 and is returned to the patient, as a result of which an optimal degassing of the liquid is achieved.

The containing body 6 has four apertures: a first inlet aperture 7 for the physiological fluid from which the gas
30 is to be separated, a second inlet aperture 8 designed to convey an infusion fluid into the containing body, an outlet or discharge aperture 9 from which the physiological fluid and any infusion fluid can pass out, and a fourth aperture 10 designed to be connected to a service line 11

for acquiring pressure information, or to be connected directly to the external atmosphere.

In greater detail, the first inlet aperture 7 is formed by a tubular element 7a which communicates with the interior 5 of the containing body and to which a tube 12 for conveying the physiological fluid can be fixed; the first inlet aperture 7 and the corresponding tubular portion 7a are positioned tangentially to the containing body.

10 The second inlet aperture 8 is spaced apart from and located above the first inlet aperture 7. It should be noted that the second inlet aperture is directed centrally towards the axis 6a of the containing body 6.

15 The discharge aperture 9, formed by a tubular channel 9a located at the lower end of the containing body, permits the progressive discharge of the blood, or of the blood mixed with the infusion liquid if required.

20 The containing body 6, whose structure is formed from two halves 13, 14 assembled together, has an active surface 15 which delimits its internal volume 16 where a guide element 17 operates.

25 The guide element 17 has its own active surface 18, with a continuous profile designed to contact and guide the fluid, as described in detail below. In practice, the guide element is a solid or internally hollow solid of rotation, designed to reduce the internal volume of the containing body that can be actually occupied by the fluid entering through the aforesaid apertures; the guide element 17 is fixed to the said body 6 by means of a support structure comprising radial supports 19 (see Figure 7), spaced apart 30 at equal angular intervals, interposed between the guide element and the containing body. The guide element extends coaxially with the body 6 and is placed above and spaced axially apart from the discharge aperture 9.

A first chamber 20, which has an essentially annular profile and into which the first inlet aperture opens directly, is thus formed between the active surface 18 of the guide element and the active surface 15 of the containing body.

The active surfaces 15 and 18 of the said containing body and the said guide element face each other and are shaped in the form of surfaces of revolution about a common axis of symmetry which is transverse with respect to the tangential direction of access of the said flow. The geometrical configuration and the relative positions of the active surfaces 15 and 18, combined with the tangential direction of the first access aperture, produce a rotary motion of the blood entering from the first aperture 7 around the guide element. This rotary motion promotes the centrifugal radial movement of the gas bubbles having a relatively low mass (< 10 microlitres), while the larger bubbles tend to accumulate in the proximity of the surface of the guide element, whose profile tends to make them move upwards towards the aperture 10.

It should be noted that the guide element 17 comprises, in detail, a central portion 21, a first terminal portion 22 facing the said discharge aperture, and a second terminal portion 23 axially opposed to the first terminal portion. The first terminal portion 22 has a cross section whose radial dimension is reduced progressively towards the said discharge aperture: in the illustrated example, the first portion is conical with its vertex facing the discharge aperture; and the second terminal portion 23 has a cross section whose radial dimension is reduced progressively away from the said discharge aperture.

In the illustrated example, the second terminal portion is also conically shaped with its vertex facing away from the discharge aperture; the central portion 21 has a cross section whose radial dimension is reduced progressively away from the said terminal portions, to form an

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intermediate area having a minimum radial dimension. More precisely, the central portion has a curved profile in longitudinal section. It is this special configuration of the central portion that makes the gas bubbles accumulating 5 on the element 17 tend to rise along a path that essentially follows the profile of the said guide element.

In other words, the guide element has a cross section with a constant profile (preferably circular) whose radial dimension first increases and then decreases from the 10 centre of the element towards the two axially opposed ends, thus forming the aforesaid conical terminal portions 22, 23.

The geometry of the containing body 6 will now be described.

15 In Figure 1 it will be noted that the active surface 15 of the body 6 is divided axially into a plurality of consecutive areas. A first area 24, having the maximum radial dimension and a constant radius, extends around the central portion 21 of the guide element. A second area 25, 20 whose radial dimension is reduced progressively towards the discharge aperture, extends consecutively to the first area 24 and essentially around the first terminal portion of the guide element. A third area 26 whose radial dimension is reduced progressively away from the discharge aperture 25 extends consecutively to the first area and essentially around the second terminal portion of the guide element, at the opposite end from the second area.

As is clearly shown in the attached figures, the first inlet aperture opens into the said first chamber 20, in the 30 said first area 24; thus the entering fluid follows a circular path and is effectively decelerated.

Because of the guide element 17, the flow in the first chamber rotates about the axis of the containing body, without being allowed to enter the central area of the said

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first chamber 20, and without giving rise to areas in which the flow velocity is zero. The absence of stagnation points and zero-velocity areas advantageously prevents the development of a siphon effect towards the discharge outlet, thus preventing a harmful return of bubbles and a practically uncontrolled motion of the fluid.

As mentioned above, the containing body also comprises a second inlet aperture 8 located above the first inlet aperture 7 and connected to a line 27 designed to carry a second fluid into the containing body. Normally, an infusion fluid can be sent through the aforesaid line 27 and introduced into the containing body to mix the fluid with the blood or other physiological fluid.

In particular, the containing body has at least a second chamber 28 located above the guide element, in an axially consecutive position and in fluid communication with the said first chamber 20 via an annular passage 29.

The second inlet aperture 8 opens directly into the said second chamber, and creates a layer of infusion liquid which extends above and in contact with the physiological fluid.

It should be noted that the second aperture is positioned with a direction of access 7b which is parallel to the direction of access 8b of the first aperture 8. In greater detail, as shown in Figures 4 and 5, the directions 7b and 8b are parallel but staggered, or in other words are located in vertical planes which are spaced apart from each other.

A mixing interface is thus formed between the physiological fluid, such as blood, present in the first chamber and the infusion liquid entering the second chamber.

The uniform and rapid mixing, and the simultaneous degassing, of the two fluids are clearly promoted by the rotary motion imparted to the physiological fluid, by the

relative positioning of the corresponding apertures 7 and 8, and by the interaction between the containing body and the guide element.

Moreover, direct contact between the air and the physiological fluid occupying the first chamber is prevented by the provision of a layer of infusion liquid in the second chamber.

In the illustrated case, if the blood or other physiological fluid flows at a rate of approximately 450 ml/min through the first aperture and a saline fluid flows at a rate of 1 ml/min through the second aperture, it is possible to produce a constant saline-blood layer with a thickness of 5-10 mm in the second chamber.

The thickness of the said layer is greater than 2 mm and smaller than the maximum diameter of the internal surface of the containing body, in order to combine effective de-airing with optimal mixing of the fluids; in the case considered here, the maximum thickness is 20 mm.

The supply of fluid along the line 27 is regulated by means of a pump 27a controlled by a control unit 36. The unit 36 is programmed to control the pump 27a and to provide a specified rate of flow for each specified time interval, in either continuous or intermittent mode. In other words, the control unit can be programmed to follow a specified constant flow rate, or a flow rate variable with time according to a specified profile, or, finally, to supply specified volumes of fluid in intermittent mode at specified time intervals.

A device for measuring the actual flow through the line 27 interacts with the control unit 36. This measuring device comprises, for example, a weighing machine 27b designed to weigh a container of liquid 27c and to send to the unit 36 information relating to the actual weight of the container

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during the treatment. Alternatively, a flowmeter interacting with the said control unit can be provided.

The control unit is capable of controlling the flow rate of the blood pump 3a and the infusion pump 27a in order to
5 ensure that a layer of infusion liquid whose thickness falls within a specified range is constantly present and is located above the blood.

Finally, the containing body includes a third chamber 30, axially consecutive to the said second chamber, and
10 designed to hold and recover the gas separated from the said fluids; the third chamber extends in the top of the containing body, above the theoretical liquid level BL.

In the illustrated example, the third chamber 30 is bell-shaped and its theoretical volume is delimited below by the
15 level BL and above by the fourth aperture, which connects the internal volume of the containing body, and particularly that of the third chamber 30, to a service line or directly to the external environment.

In the illustrated example, a service line 11 is provided,
20 with a first end 11a placed in fluid communication with the said third chamber 30, and a second end 11b connected for operation to a pressure sensor element 31.

As an alternative to what is described above, the pressure sensor element 34 can be made to operate down-line from the
25 device 1.

At least one hydrophobic membrane 32 is associated for operation with an intermediate area 11c of the service line to prevent the access of liquid to the pressure sensor (if present) and to ensure sterile separation between the
30 machine side and the side in which the physiological fluid is present and circulates.

The third chamber has a volume such that any increase in pressure in a range from a minimum value to a maximum value

of pressure (from 100 to 350 mmHg, for example) does not cause any penetration of liquid into the service line 11, but instead leaves a constant gas space in the third chamber.

- 5 It should be noted that different operating modes can be provided to control the level of the gas that is progressively separated from the fluids or that reaches the device 1 in any way.

1 - Fully manual mode.

- 10 At least one access site 33 can be provided in the service line 11, to enable a user to draw off gas in a fully manual way (by means of a syringe).

2 - Semiautomatic mode.

- 15 The service line 11 is connected to the pressure sensor 31, which is connected down-line to a solenoid valve 34 and to an air pump 35. The valve and the pump can be used to send gas to, or to draw gas from, the service line. If the operating level of the liquid to be maintained in the containing body is indicated by BL, the user can control 20 the pneumatic pump and valve circuit, using a keypad for example, to move the level in one or other direction until BL is reached.

3 - Automatic mode.

- 25 For operation in fully automatic mode, use is made of a liquid level sensor LLS, of the optical, ultrasonic or other type for example. The sensor LLS is located above the level BL. The level sensor LLS can operate at or near the top of the containing body; alternatively, the level sensor LLS can be made to operate in a section of the tubing 11a, 30 for example in a terminal area of the tubing, essentially next to the fourth aperture 10 as shown in Figure 1. A control unit 36 is connected to the sensor LLS and operates the pump 35 and the solenoid valve 34, in order to maintain

the liquid level in the vicinity of BL. In greater detail, the control unit can order the execution of the following steps:

- if LLS signals the presence of liquid:
 - 5 a) activation of the pump 35 to drive towards the third chamber a volume V_1 , equal to the volume between LLS and the fourth aperture;
 - b) activation of the pump 35 to draw gas from the third chamber while LLS continues to signal the presence of liquid;
 - 10 c) activation of the pump 35 to drive towards the third chamber a volume of liquid V_2 , equal to $V_1 + V_c$, where V_c is the volume of the third chamber.
- if LLS does not signal the presence of liquid, then the aforementioned three steps a), b) and c) are repeated automatically in succession at specified time intervals.

It should be noted that the automatic procedure described above has the significant advantage of not allowing liquid to remain stationary in the section in which the sensor LLS operates. This is rather important because the upper layer of liquid, even in the presence of a saline infusion injected through the second aperture, always contains a certain percentage of cellular material which, in the long term, can generate encrustations which adversely affect the correct operation of the sensor LLS and consequently the efficient monitoring of the liquid level.

It should also be noted that the described level monitoring procedure prevents the flow of liquid towards the service line 11, thus providing a further means of ensuring safety and guaranteeing the absolute sterility of the fluid present in the device 1.

CLAIMS

1. Gas separation device for a physiological fluid, comprising:
 - a containing body having an internal active surface and having at least a first inlet aperture for a physiological fluid, positioned with a tangential direction of access, and at least one outlet aperture for the said fluid, spaced apart from the said inlet aperture; characterized in that it comprises:
 - 5 - a guide element housed at least partially within the said body and having a continuous active surface designed to contact and guide the said fluid;
 - a first annular chamber formed between the active surface of the said guide element and the internal active surface of the said containing body.
- 10 2. Device according to claim 1, characterized in that the said inlet aperture opens directly into the said first chamber.
- 15 3. Device according to claim 1, characterized in that the said guide element is wholly housed within the containing body, extends coaxially with the latter and is spaced axially apart from the said outlet aperture.
- 20 4. Device according to claim 3, characterized in that the active surfaces of the said containing body and of the said guide element face each other and are shaped in the form of surfaces of revolution about a common axis of symmetry which is transverse with respect to the tangential direction of access of the said flow.
- 25 5. Device according to claim 1, characterized in that the said outlet aperture is positioned in a lower end of the said containing body, the said guide element and

the said first chamber extending above the said outlet aperture.

6. Device according to claim 1, characterized in that the said guide element is a solid or internally hollow solid of rotation, designed to reduce the volume of at least the said first chamber.
5
7. Device according to claim 1, characterized in that the said guide element comprises:
 - a central portion;
 - 10 - a first terminal portion, facing towards the said outlet aperture; and
 - a second terminal portion, axially opposed to the first terminal portion and facing towards a second chamber extending above the said guide element.
- 15 8. Device according to claim 7, characterized in that the first terminal portion has a cross section whose radial dimension is reduced progressively towards the said outlet aperture.
9. Device according to Claim 8, characterized in that the
20 said first terminal portion has a conical shape with its vertex facing towards the outlet aperture.
10. Device according to Claim 7, characterized in that the second terminal portion has a cross section whose radial dimension is reduced progressively away from the
25 said outlet aperture.
11. Device according to Claim 10, characterized in that the said second terminal portion has a conical shape with its vertex opposed to the outlet aperture.
12. Device according to Claim 7, characterized in that the
30 central portion has a cross section with a radial dimension which is reduced progressively away from the

said terminal portions, to form an intermediate area having a minimum radial dimension.

13. Device according to Claim 12, characterized in that the central portion has a curved profile in longitudinal section.
14. Device according to Claim 7, characterized in that the said active surface of the containing body has:
 - a first area, of maximum radial dimension, extending around the central portion of the guide element;
 - 10 - a second area, whose radial dimension is reduced progressively towards the outlet aperture, the second area extending consecutively to the first area and essentially around the first terminal portion of the guide element;
 - 15 - a third area, whose radial dimension is reduced progressively away from the outlet aperture, the third area extending consecutively to the first area and essentially around the second terminal portion of the guide element.
- 20 15. Device according to Claim 14, characterized in that the first inlet aperture opens into the said first chamber, in the said intermediate first area of the active surface of the containing body.
- 25 16. Device according to Claim 14, characterized in that the first area of the active surface has a constant radius.
17. Device according to Claim 1, characterized in that the said containing body comprises a second inlet aperture located above the said first inlet aperture and designed to convey a second fluid into the containing body.
- 30 18. Device according to Claim 17, characterized in that it comprises a second chamber extending above the said

guide element, in an axially consecutive position and in fluid communication with the said first chamber and with the said second inlet aperture.

19. Device according to Claim 18, characterized in that the
5 said second inlet aperture opens directly into the said second chamber, preferably in a direction parallel to, and staggered with respect to, that of the said first inlet aperture.
20. Device according to Claim 18, characterized in that the
10 said containing body includes a third chamber, which is axially consecutive to the said second chamber and which is designed to contain the gas separated from the said fluids, the said third chamber extending in the top of the said containing body.
21. Device according to Claim 20, characterized in that it
15 comprises at least one service line having a first end which is brought into fluid communication with the said third chamber by means of a fourth aperture formed in the said containing body.
22. Device according to Claim 21, characterized in that it
20 comprises at least one pressure sensor element associated for operation with the said service line.
23. Device according to Claim 21, characterized in that it
25 comprises at least one hydrophobic membrane associated for operation with an intermediate area of the service line.
24. Device according to Claim 21, characterized in that the
third chamber has a nominal volume V_c delimited below by a theoretical maximum level line BL and above by the
30 said fourth aperture.
25. Device according to Claim 21, comprising a pneumatic circuit operating in the said service line, for

selectively sending gas to the service line and drawing gas from it.

26. Device according to Claim 25, comprising a liquid level sensor LLS located above a level BL, and a control unit connected to the sensor LLS and designed to control the said pneumatic circuit to maintain the liquid level in the vicinity of the said level BL.
- 5
27. Device according to Claim 26, in which the level sensor LLS operates in a section of the service line and in which the said control unit is designed to cause the execution of the following steps:
- 10
- determining whether LLS is signalling the presence of liquid, and, if so, executing the following sub-steps in sequence:
- 15
- a) activation of the pneumatic circuit to drive towards the third chamber a volume V_1 , equal to the volume between the section in which LLS operates and the fourth aperture;
- 20
- b) activation of the pneumatic circuit to draw gas from the third chamber while LLS continues to signal the presence of liquid,
- 25
- c) activation of the pneumatic circuit to drive towards the third chamber a volume of liquid V_2 , equal to $V_1 + V_c$, where V_c is the volume of the third chamber;
- if, on the other hand, LLS is not signalling the presence of liquid, executing the aforementioned three steps a), b) and c) at specified time intervals.
28. Device according to Claim 21, characterized in that it comprises at least one access site located in the said service line for manually drawing fluid from the said line or sending fluid into it.
- 30

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29. Device according to Claim 26, characterized in that the level sensor LLS can operate on the said containing body.
30. Device according to Claim 1, characterized in that it comprises:
- a first line for sending the physiological fluid into the said containing body through the first inlet aperture,
 - a second line for sending a second fluid into the said containing body through a second inlet aperture,
 - a pump operating to create a flow along the first line,
 - a pump operating to create a flow along the second line,
 - a control unit programmed to control the pumps operating in the first and second lines and to ensure the constant presence in the containing body of a layer of the said second fluid whose thickness lies within a specified range, this layer being located above the physiological fluid.
31. Fluid mixing device with gas separation, comprising a containing body having an internal active surface and having at least one first inlet aperture for a physiological fluid, and at least one fluid outlet aperture, spaced apart from the said first inlet aperture, characterized in that the containing body has at least one second inlet aperture located above the said first inlet aperture and designed to convey a second fluid into the containing body to form a layer of the said second fluid above the said physiological fluid.
32. Device according to Claim 31, characterized in that the said containing body includes:

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- at least a first chamber extending in a lower area of the containing body and in fluid communication with the said outlet aperture;
 - at least a second chamber, extending in an axially consecutive upper area and in fluid communication with the said first chamber.
- 5
33. Device according to Claim 32, characterized in that the said containing body includes a third chamber, which is axially consecutive to the said second chamber and which is designed to contain the gas separated from the said fluids, the said third chamber extending in the top of the said containing body and having a fourth aperture.
- 10
34. Device according to Claim 33, characterized in that it comprises at least one service line having a first end which is brought into fluid communication with the said third chamber by means of the fourth aperture formed in the said containing body.
- 15
35. Device according to Claim 34, characterized in that it comprises at least one pressure sensor element associated for operation with the said service line.
- 20
36. Device according to Claim 35, characterized in that it comprises at least one hydrophobic membrane associated for operation with an intermediate area of the service line, between the fourth aperture and the pressure sensor element.
- 25
37. Device according to Claim 33, characterized in that the third chamber has a nominal volume V_c delimited below by a theoretical maximum level line BL and above by the said fourth aperture.
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38. Device according to Claim 34, comprising a pneumatic circuit for selectively sending gas to the service line and drawing gas from the line.

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39. Device according to Claim 38, comprising a liquid level sensor LLS located above a level BL, and a control unit connected to the sensor LLS and designed to control the said pneumatic circuit to maintain the liquid level in
5 the vicinity of the said level BL.
40. Device according to Claim 39, in which the said level sensor is located in the said service line and the said control unit is designed to cause the execution of the following steps:
- 10 - determining whether LLS is signalling the presence of liquid, and, if so, executing the following sub-steps in sequence:
- 15 a) activation of the pneumatic circuit to drive towards the third chamber a volume V_1 , equal to the volume between the section in which LSS operates and the fourth aperture,
- b) activation of the pneumatic circuit to draw gas from the third chamber while LSS continues to signal the presence of liquid,
- 20 c) activation of the pneumatic circuit to drive towards the third chamber a volume of liquid V_2 , equal to $V_1 + V_c$, where V_c is the volume of the third chamber;
- 25 - if, on the other hand, LLS is not signalling the presence of liquid, executing the aforementioned three steps a), b) and c) at specified time intervals.
41. Device according to Claim 34, characterized in that it comprises at least one access site located in the said service line for manually drawing fluid from the line or sending fluid to it.
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42. Device according to Claim 39, characterized in that the level sensor LLS operates on the said containing body.

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43. Device according to Claim 31, characterized in that it comprises:

- a first line for sending the physiological fluid into the said containing body through the first inlet aperture,
- a second line for sending the second fluid into the said containing body through the second inlet aperture,
- a pump operating to create a flow along the first line,
- a pump operating to create a flow along the second line,
- a programmable control unit for controlling the pumps operating in the first and second lines and for ensuring the constant presence in the containing body of a layer whose thickness lies within a specified range, this layer being located above the physiological fluid.

44. Device according to Claim 43, characterized in that the control unit activates the pump operating in the said second line in a continuous or intermittent mode, to provide a specified flow rate at every specified time interval.

45. Device according to Claim 43, characterized in that it comprises a means for sensing the actual flow in the second line, this sensor means sending corresponding signals to the said control unit.

46. Device according to Claim 43, in which the thickness of the said layer is smaller than the maximum diameter of the internal surface of the containing body.

47. Device according to Claim 32, in which the said first inlet aperture opens directly into the said first chamber in a tangential direction of access, and in which the said second inlet aperture opens directly

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towards the said second chamber in a direction of access parallel to that of the said first aperture.

48. Device according to Claim 47, comprising a guide element housed at least partially within the said body and having a continuous active surface designed to contact and guide the said fluid, the said first chamber having an annular configuration and being formed between the active surface of the said element and the active surface of the containing body.
- 5 49. Device according to Claim 48, characterized in that the said guide element is wholly housed within the containing body, extends coaxially with the latter and is spaced axially apart from the said outlet aperture.
- 10 50. Device according to Claim 48, characterized in that the active surfaces of the said containing body and of the said guide element face each other and are shaped in the form of surfaces of revolution about a common axis of symmetry which is transverse with respect to the tangential direction of access of the said flow.
- 15 51. Device according to Claim 48, characterized in that the said outlet aperture is positioned in a lower end of the said containing body, the said guide element and the said first chamber extending above the said outlet aperture.
- 20 52. Device according to Claim 50, characterized in that the said guide element is a solid or internally hollow solid of rotation, designed to reduce the volume of at least the said first chamber.
- 25 53. Device according to Claim 48, characterized in that the said guide element comprises:
30 - a central portion;

- a first terminal portion, facing towards the said outlet aperture; and
 - a second terminal portion, axially opposed to the first terminal portion and facing towards the said second chamber.
- 5 **54.** Device according to Claim 53, characterized in that the first terminal portion has a cross section whose radial dimension is reduced progressively towards the said outlet aperture.
- 10 **55.** Device according to Claim 54, characterized in that the said first terminal portion has a conical shape with its vertex facing towards the outlet aperture.
- 15 **56.** Device according to Claim 53, characterized in that the second terminal portion has a cross section whose radial dimension is reduced progressively away from the said outlet aperture.
- 19 **57.** Device according to Claim 56, characterized in that the said second terminal portion has a conical shape with its vertex opposed to the outlet aperture.
- 20 **58.** Device according to Claim 53, characterized in that the central portion has a cross section with a radial dimension which is reduced progressively away from the said terminal portions, to form an intermediate area having a minimum radial dimension.
- 25 **59.** Device according to Claim 58, characterized in that the central portion has a curved profile in longitudinal section.
- 29 **60.** Device according to Claim 53, characterized in that the said active surface of the containing body has:
- 30 - a first area, of maximum radial dimension, extending around the central portion of the guide element;

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- a second area, whose radial dimension is reduced progressively towards the outlet aperture, the second area extending consecutively to the first area and essentially around the first terminal portion of the guide element;
 - a third area, whose radial dimension is reduced progressively away from the outlet aperture, the third area extending consecutively to the first area and essentially around the second terminal portion of the guide element.
61. Device according to Claim 60, characterized in that the first inlet aperture opens into the said first chamber, in the said intermediate first area.
62. Device according to Claim 60, characterized in that the first area of the active surface has a constant radius.
63. Fluid mixing method with gas separation, comprising the following steps:
- providing a containing body having an internal active surface and having at least a first inlet aperture, at least one fluid outlet aperture spaced apart from the said first inlet aperture, and at least a second inlet aperture located above the said first inlet aperture;
 - sending a first physiological fluid into the containing body through the said first aperture;
 - conveying a second fluid into the containing body through the said second aperture to form a layer of the said second fluid above the said physiological fluid;
 - conveying a separated gas from the said first and second fluids above the said layer.
64. Method according to Claim 63, characterized in that it comprises the steps of:

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- measuring the flow rate of the said first fluid;
- measuring the flow rate of the said second fluid;
- regulating the flow rate of the said first and the said second fluid to provide a layer of the said second fluid with a thickness lying within a specified range.

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65. Method according to Claim 64, characterized in that the said second fluid is sent, in continuous or intermittent mode, in a direction of access to the containing body parallel to that of the said first fluid.

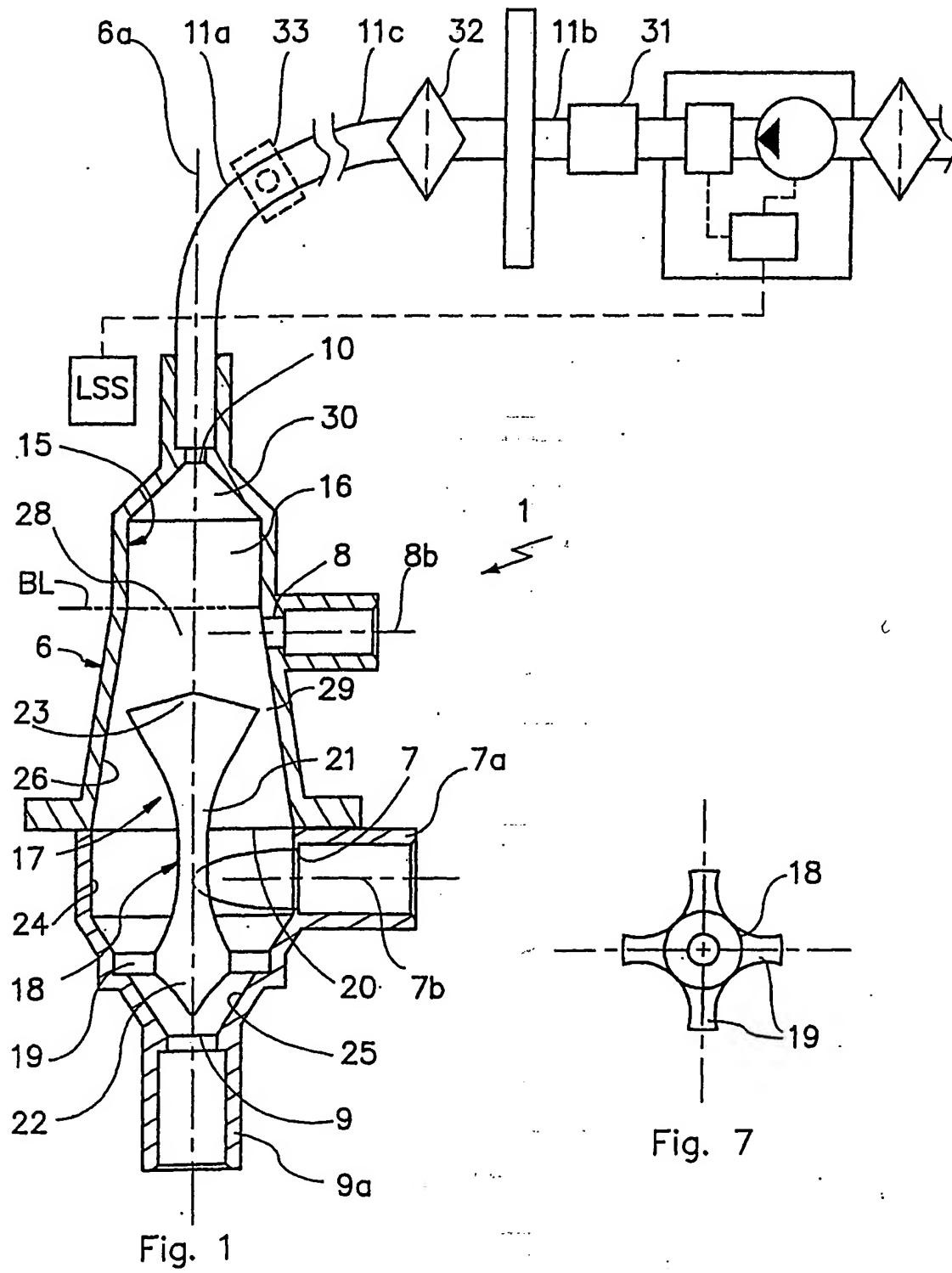
66. Method according to Claim 64, characterized in that the thickness of the said layer is kept below the maximum diameter of the internal surface of the containing body.

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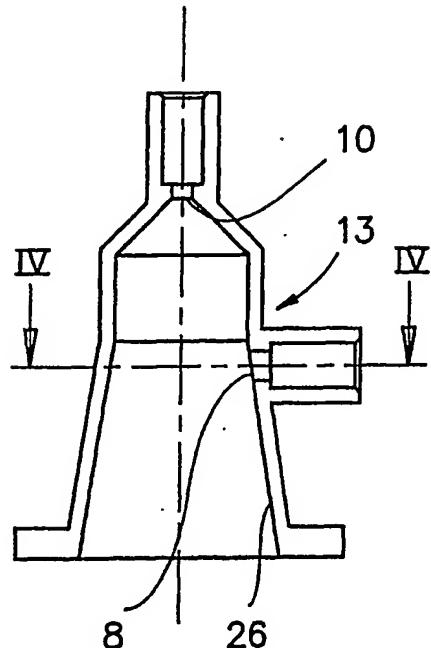


Fig. 2

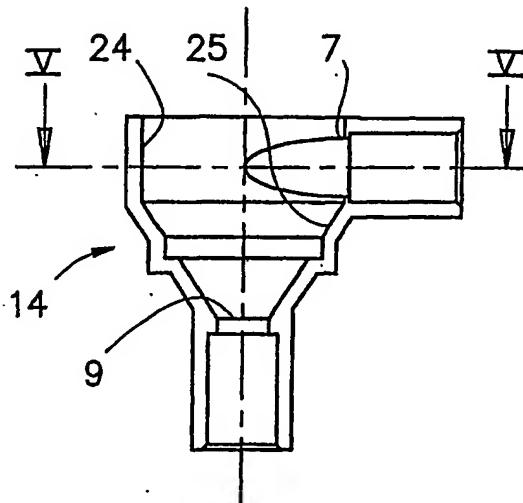


Fig. 3

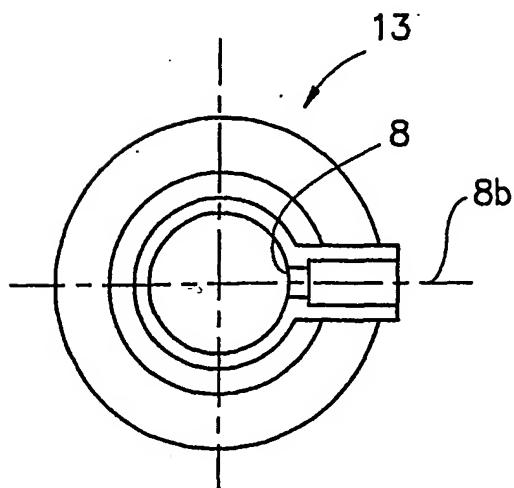


Fig. 4

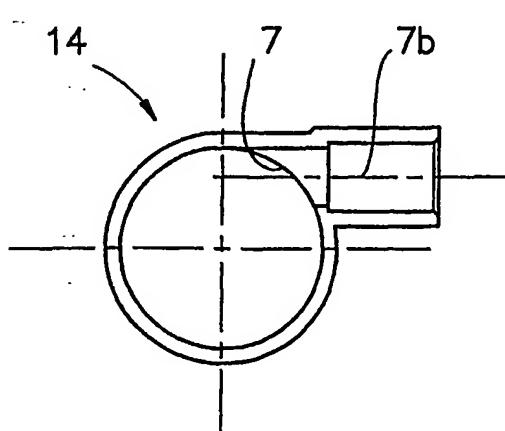


Fig. 5

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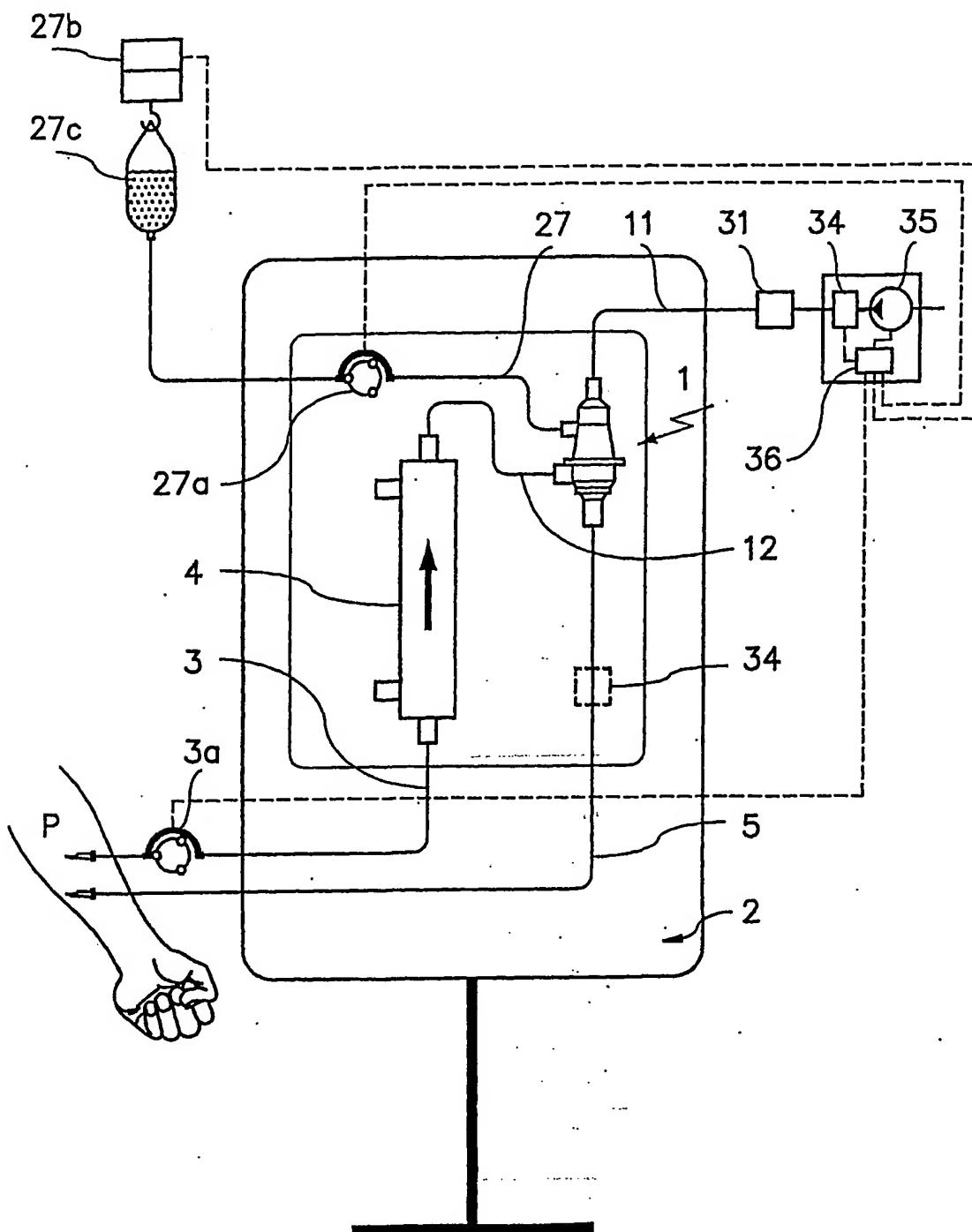


Fig. 6

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/02281

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61M1/36 B01D19/00 B01F5/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61M B01F B01D B04C		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 806 135 A (SIPOSS GEORGE G) 21 February 1989 (1989-02-21) column 4, line 53 -column 5, line 40; figures 5,6	1,3-8, 10,11, 14,16
X	EP 1 084 722 A (TERUMO CORP) 21 March 2001 (2001-03-21) paragraph '00381; figure 1	1-7,10, 11
X	US 5 707 431 A (ELLSWORTH JAMES R ET AL) 13 January 1998 (1998-01-13) cited in the application column 2, line 28 - line 54; figure 2	1-5,7
	-/-	
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		<input checked="" type="checkbox"/> Patent family members are listed in annex.
<p>* Special categories of cited documents :</p> <p>'A' document defining the general state of the art which is not considered to be of particular relevance</p> <p>'E' earlier document but published on or after the International filing date</p> <p>'L' document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>'O' document referring to an oral disclosure, use, exhibition or other means</p> <p>'P' document published prior to the international filing date but later than the priority date claimed</p> <p>'T' later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>'&' document member of the same patent family</p>		
Date of the actual completion of the International search 5 November 2003	Date of mailing of the International search report 17.11.2003	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx. 31 651 epo nl Fax (+31-70) 340-3016	Authorized officer Lakkis, A	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 03/02281

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

International Application No. PCT/IB 03 A2281

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-16

Gas separation device comprising a containing body having a first inlet aperture, further comprising a guide element and a first annular chamber characterized in that:

- 1.1 the inlet aperture opens directly into said first chamber
- 1.2 said guide element is wholly housed within the body
- 1.3 said outlet aperture is positioned in a lower end of said body
- 1.4 said guide element is a solid of rotation
- 1.5 said guide element comprises three portions

2. Claims: 17-66

Gas separation device comprising a containing body having a first inlet aperture, further comprising a guide element and a first annular chamber, characterized in that the containing body comprises a second inlet aperture;

Fluid mixing device with gas separation, comprising a containing body having a first inlet aperture, characterized in that the containing body comprises a second inlet aperture; further associated mixing method

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/02281

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 1 506 555 A (JOHNSON & JOHNSON) 5 April 1978 (1978-04-05) page 4, line 6 - line 46; figure 5	31,32,63
A		17,30
X	US 5 935 093 A (VAN DRIEL MICHAEL R ET AL) 10 August 1999 (1999-08-10) column 2, line 13 -column 3, line 31; figure 3AB	31,32,63
A		17,30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Filing No
PCT/IB 03/02281

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 4806135	A	21-02-1989	NONE		
EP 1084722	A	21-03-2001	US	6451257 B1	17-09-2002
			EP	1084722 A2	21-03-2001
			JP	2001129081 A	15-05-2001
US 5707431	A	13-01-1998	CA	2142413 A1	16-08-1995
			CN	1116956 A	21-02-1996
			EP	0676213 A2	11-10-1995
			JP	2796259 B2	10-09-1998
			JP	8113979 A	07-05-1996
			JP	7328317 A	19-12-1995
GB 1506555	A	05-04-1978	CA	1069793 A2	15-01-1980
			DE	2523236 A1	11-12-1975
			FR	2271857 A1	19-12-1975
			GB	1505901 A	05-04-1978
			IT	1040598 B	20-12-1979
			JP	51000195 A	05-01-1976
US 5935093	A	10-08-1999	NL	7505979 A	26-11-1975
			AU	9676398 A	23-04-1999
			WO	9916483 A1	08-04-1999